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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/193,538	11/17/1998	PATRICIA A. BILLING-MEDEL	6193.US.P1	2144

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ABBOTT LABORATORIES
DEPT. 377 - AP6D-2
100 ABBOTT PARK ROAD
ABBOTT PARK, IL 60064-6050

EXAMINER	
SOUAYA, JEHANNE E	

ART UNIT	PAPER NUMBER
1634	24

DATE MAILED: 08/19/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/193,538	Applicant(s) BILLING-MEDEL ET AL.	
	Examiner Jehanne Souaya	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 June 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-37,39,40,42-44,50-54,56-58,60-63,65-70 and 72-78* is/are pending in the application.

4a) Of the above claim(s) *23-37,39,40,42-44,50 and 51* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *52-54,56-58,60-63,65-70 and 72-78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Currently, claims 23-37, 39-40, 42-44, 50-54, 56-58, 60-63, 65-70, and 72-78 are pending in the instant application. Claims 23-37, 39-40, 42-44, and 50-51 are withdrawn from consideration as being directed to non elected subject matter from a previous restriction requirement. Claims 55, 59, 64, and 71 have been canceled. Claims 52-54, 56-58, 60-63, 65-70, and 72-78 are currently under examination. All the amendments and arguments have been thoroughly reviewed but are deemed insufficient to place this application in condition for allowance. Any rejections not reiterated are hereby withdrawn. The following rejections are reiterated. They constitute the complete set being presently applied to the instant Application. Response to Applicant's arguments follow. This action is FINAL.

2. The cancellation of claims 55, 59, and 64 has rendered the rejection of these claims under 35 USC 112/first paragraph (page 8 of the previous office action) moot.

3. The cancellation of claim 71 and the amendment of claim 78 have obviated the rejection of these claims regarding "epitope" under 35 USC 112/first paragraph, written description. Upon further review of the specification, specifically, p. 55, lines 12-14, which teaches that SEQ ID NO 7 encodes an open reading frame, the rejection of claims 52-78 under 35 USC 112/first paragraph, written description (at page 13 of the previous office action) is withdrawn. Neither the specification nor the art provide any basis to question that the open reading frame contained in SEQ ID NO 7 is a full length open reading frame and the rejection is withdrawn based on the fact that the examiner interprets the teaching in the specification to be that the "open reading

frame encoding a 188 residue amino acid sequence which is presented as SEQ ID NO 17" is a full length open reading frame.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Maintained Rejections

Claim Rejections - 35 USC § 101

5. Claims 52-54, 56-58, 60-63, 65-70, and 72-78 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by a specific or substantial asserted utility, or a well established utility.

The claims are drawn to polynucleotides having a sequence selected from the group consisting of SEQ ID NOS 1-7, to methods of detecting a target polynucleotide using the polynucleotides of SEQ ID NOS 1-7, and to kits comprising these polynucleotides.

The specification teaches the general utility for the invention is detection of the gene product itself in a sample (p. 10 of the specification). This is not deemed to be specific as this utility is applicable to polynucleotides in general. The specification asserts that the polynucleotides of the invention can be used to detect, amplify, or quantify genes, nucleic acids, cDNAs or mRNAs relating to breast tissue disease and conditions associated therewith (p. 25). The specification further asserts that the compositions and methods described in the specification will enable the identification of certain markers as indicative of breast tissue disease or condition

wherein this information will aid in, for example, detecting conditions associated with BS274, especially breast cancer (p. 10-11, bridging paragraph). However this is assertion is not deemed to be substantial as the specification does not teach the specific role of BS274 in breast cancer, nor has the specification demonstrated that BS274 is a marker for breast disease, especially breast cancer. From the teachings in the specification, it is evident that neither the function nor the role of BS274 in association with breast disease or breast cancer was known at the time the invention was filed. At page, 11, lines 6-12, the specification states "It is also *thought* that the polynucleotides or polypeptides and protein encoded by the BS274 gene are useful as a marker. This marker is either elevated in disease such as breast cancer, altered in disease such as breast cancer, or present as a normal protein but appearing in an inappropriate body compartment." The specification only teaches that the BS274 consensus sequence was found more than 28 more times in breast tissue libraries than non breast tissue libraries (p 54), but does not demonstrate that BS274 is a marker for breast cancer (analysis to follow). Therefore, while the BS274 consensus sequence is found to be present to a greater extent in breast tissue, this is not considered a "real world" use for the claimed polynucleotides, kits, or methods of using the polynucleotides of the claimed invention. Further experimentation would be required to determine whether the elevated presence of the BS274 consensus sequence, whether the presence of altered BS274, or whether the presence of BS274 in an inappropriate body compartment is indicative of breast disease or breast cancer. The specification also does not provide any teachings as to the function of the protein encoded by BS274.

At page 54, the specification teaches that ESTs were derived from cDNA libraries made from breast tumor tissues, breast non-tumor tissues and numerous other tissues, both tumor and non tumor and entered into a database. The specification teaches that the transcript images were evaluated to identify ESTs that were representative primarily of breast tissue libraries, and that these ESTs were ranked, giving an EST corresponding to the consensus sequence of BS274 (SEQ ID NO 7) which was found in 23% of breast tissue libraries (p. 62). The specification teaches that the consensus sequence (SEQ ID NO 7) or fragments thereof (SEQ ID NOS 1-6) were found more than 28 more times in breast than non breast tissues. However, while the consensus sequence expression appears to be more prevalent in breast tissue, the specification has not demonstrated that BS274 is specific for breast tumor tissue. The specification only teaches that the BS274 consensus sequence was found 28 more times in breast than non breast libraries, but does not teach the ratio of BS274 in normal breast vs. breast tumor tissues. Thus while the specification *suggests* that SEQ ID NOS 1-7 can be used to detect nucleic acids relating to breast tissue disease the specification does not demonstrate such. Furthermore, at page 62, the specification teaches upon hybridization with a BS274 probe, northern analysis revealed an approximately 860 nucleotide band in the RNA of 5 out of 5 normal breast tissue samples was found. While the specification also taches that the band was found in 2 of 2 breast cancer tissue samples, the specification does not teach whether a difference in expression levels was found between breast cancer tissue and non breast tissue. Thus while the specification *suggests* that

SEQ ID NOS 1-7 can be used to detect nucleic acids relating to breast tissue disease the specification does not demonstrate such.

Claim Rejections - 35 USC § 112

Enablement

6. Claims 52-54, 56-58, 60-63, 65-70, and 72-78 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. The specification teaches that the compositions and methods described herein will enable the identification of certain markers as indicative of a breast tissue disease or condition, and that the information obtained therefrom will aid in the detecting, diagnosing, staging, monitoring, prognosis, in vivo imaging, preventing or treating diseases of the breast, however the specification does not teach having done so. However, it cannot be determined from the teachings in the specification, and the art is silent as to, what the biological function of the polypeptides encoded by the sequences of SEQ ID NOS 1-7 and also as to how these polynucleotides or polypeptides are correlated to or would be useful in detecting any breast tissue diseases. Therefore, the skilled artisan would have to perform undue experimentation to determine the function of the polypeptides encoded by the sequences of SEQ ID NOS 1-7 or to determine whether the presence of these polynucleotides is associated with breast cancer or any breast disease.

Response to Arguments

7. The response traverses the rejections made under 35 USC 101 and 112/first paragraph in the same section (pages 3-5 of response filed June 5, 2002. Applicant submitted a gel in the preliminary amendment filed 9/17/2001 that showed strong expression of BS274 in breast tumor tissue and breast cancer cell line T47D. The gel shows faint bands in lanes which are colon tumor, lung tumor, and ovary tumor. The response asserts that these results illustrate the upregulation of BS274 in breast tumors and that the evidence further demonstrates that BS274 can be used to determine the origin of a tumor in a patient. The response asserts that tissue specific markers, such as BS274 are useful in identifying the site of origin of a particular cancer which is critical so that a clinician can determine the appropriate course of clinical treatment for that cancer. The response cites a translated abstract from a Spanish publication (Anales de medicina interna 17(11): 603-608, November 2000 as evidence of the problem that it is very difficult for clinicians to determine the origin of a tumor that is found in a metastatic site. This argument has been thoroughly reviewed but was found unpersuasive. The gel submitted by applicant's illustrates that a BS274 is expressed more strongly in breast tumor tissue and a breast cancer cell line over other cancers. The gel, however, does not demonstrate that a BS274 marker is overexpressed or upregulated in a secondary site, such as lung, liver, or bone as a result of breast cancer metastasis. The translated abstract submitted by applicants was also thoroughly reviewed but was not found persuasive as illustrative of a well established utility for the claimed

SEQ ID NOS because the abstract does not indicate that any transcript, let alone SEQ ID NOS 1-7 of the claimed invention, that are overexpressed in normal breast libraries as well as breast tumor libraries can be used to determine the cite of primary origin of a tumor. It is also noted that the reference was published in November of 2000, while the instant application was filed 11/17/1998, therefore the reference would not be indicative of a well established utility at the time of applicants invention. It is also noted that the utility submitted by applicant's in the response filed 6/5/2002 was not asserted in the specification. With regard to applicants assertion that BS274 has a specific and substantial utility in that it can be used to identify a tumor as coming from a breast and not from other locations of the body such as the colon, lung or ovary, the same can be said of any transcript that is overexpressed in breast tumor and normal breast library and is not specific to the claimed polynucleotides. The specification has not demonstrated that BS274 is a breast tumor marker because the specification only teaches that BS274 transcripts were detected 28 more times in normal breast and breast tumor tissue over other tissues. This only demonstrates that BS274 is a breast specific marker. The gel submitted in the preliminary amendment of 9/17/2001 does not demonstrate that BS274 is a breast tumor marker because, in light of the teachings in the specification, it does not include a comparison of normal breast tissue vs breast tumor tissue. For these reasons and the reasons made above, and in previous actions, the rejections made under 35 USC 101 and 112/first paragraph are maintained.

Conclusion

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. No claims are allowable.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Souaya whose telephone number is (703)308-6565. The examiner can normally be reached Monday-Friday from 9:00 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jehanne Souaya

Jehanne Souaya
Patent examiner
Art Unit 1634
August 15, 2002

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600